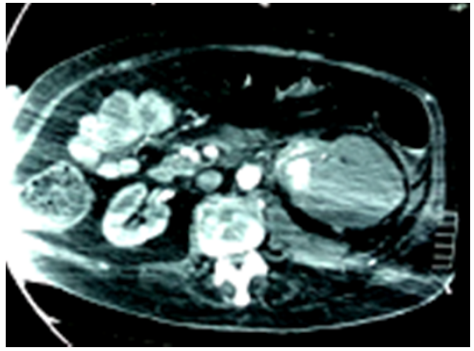
Giovanni Lanfranco's Saint Luke Healing the Dropsical Child (c. 1625)

Διαφορική Διάγνωση

Τότσικας Χαρίσης
Επιμελητής Β'
Ε' Παθολογική Κλινική-
Μονάδα Ειδικών Λοιμώξεων

Ο ασθενής …

Ανεύρυσμα αριστερής νεφρικής αρτηρίας



N Engl J Med 2014; 371:e11August 21, 2014

Χαρακτηριστικά ανευρύσματος νεφρικής αρτηρίας (RAA)

Incidence	• Autopsy rates, <0.01%-0.09% • Arteriogram rates, 0.3%-2.5% (up to 9.7%) • CT rates, 0.7%
Natural history	• Large autopsy series demonstrate no rupture • Most report no rupture during surveillance out to 270 months • Growth rate 0.06-0.6 mm/y • Rupture rate 3%-5% with nongestational mortality <10%
Clinical presentation and risk factors	• Sixth decade of life (range, 46-62 years of life) • Female predominance up to 72% • Association with FMD up to 68% • Symptoms rare (4%-23%): abdominal and/or flank pain, hematuria • Clinical exam may identify: HTN, renal bruit, and palpable abdominal mass • Majority of patients are hypertensive • Chronic renal insufficiency has been identified in 4-14% of patients • Alternate arterial aneurysms (ie, aortic, iliac, visceral) in 7%-30% of cases
Anatomy and radiographic features	• Most saccular • Two-thirds affect arterial bifurcations • Often multiple, 10%-20% bilateral, non-renal arterial aneurysms (7%-30%) • 18%-68% calcified • 8%-11% demonstrate thromboembolism

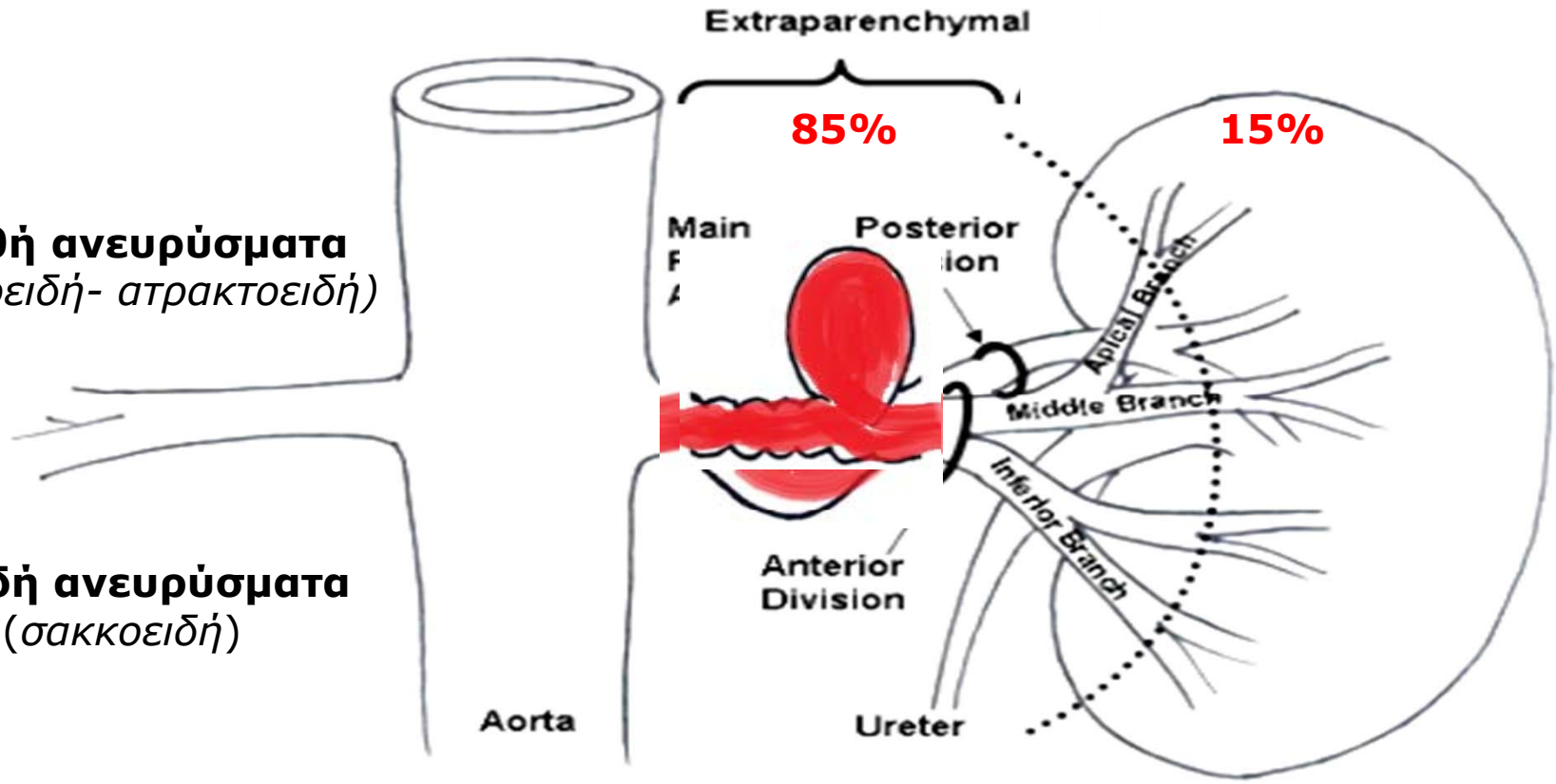
CT, Computed tomography; *FMD,* fibromuscular dysplasia; *HTN,* hypertension.

Coleman DM, Stanley JC; J Vasc Surg.2015 Sep;62(3):779-85

Ανεύρυσμα νεφρικής αρτηρίας (RAA)

Αληθή ανευρύσματα
(σακκοειδή- ατρακτοειδή)

Ψευδή ανευρύσματα
(*σακκοειδή*)



Το τοίχωμα του αποτελείται από τον έξω χιτώνα της αορτής και τον περιαορτικό ινώδη ιστό, ή από εξαγγειωμένο αίμα, που σχηματίζει την κοιλότητα του ψεύδους ανευρύσματος.

Συμμετέχουν όλες οι στιβάδες του τοιχώματος της αρτηρίας

Ανεύρυσμα νεφρικής αρτηρίας (RAA)

Αληθή ανευρύσματα

- Ινομυώδης δυσπλασία
- Σύνδρομο *Ehlers– Danlos*

Ενδοπαρεγχυματικά

- Οζώδης πολυαρτηρίτιδα
- Νευροϊνωμάτωση

Ψευδή ανευρύσματα

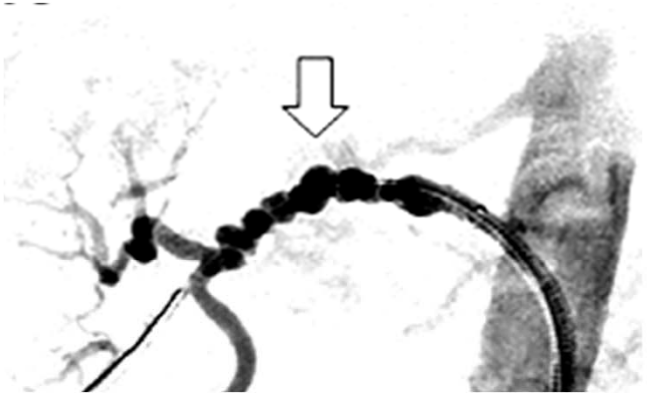
- Τραύμα
- Ιατρογενή
- Αυτόματο
- Διαχωρισμός
- Μυκωτικό
- Νόσος Kawasaki

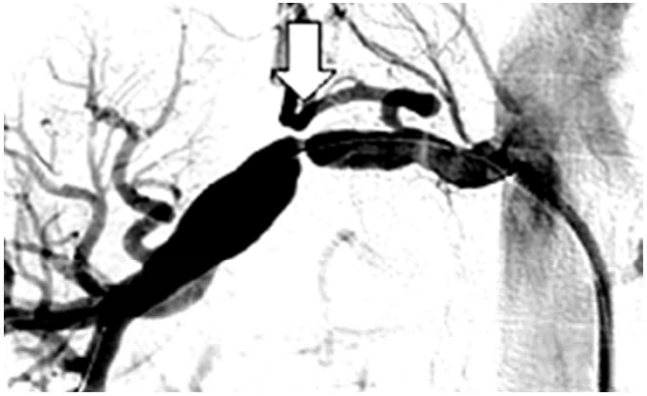
Αληθή ανευρύσματα

- Ινομυώδης δυσπλασία
- Σύνδρομο *Ehlers– Danlos*

Ινομυώδης Δυσπλασία (FMD)

Ιδιοπαθής, μη αθηροσκληρωτική, μη φλεγμονώδης νόσος που χαρακτηρίζεται από ανώμαλο κυτταρικό πολλαπλασιασμό και διαταραχές της αρχιτεκτονικής του τοιχώματος της αρτηρίας (μεσαίου- μικρού μεγέθους)





- Hypertensive patients < 30 years of age, especially women
- Accelerated, malignant, or grade 3 (> 180/110 mmHg) hypertension
- Drug-resistant hypertension (blood pressure target not achieved despite 3 drug-therapy at optimal doses including a diuretic)
- Unilateral small kidney without a causative urological abnormality
- Abdominal bruit in the absence of atherosclerotic disease or risk factors for atherosclerosis
- Suspected renal artery dissection/infarction
- Presence of FMD in at least one other vascular territory

Gornik, Persu et al.; Journal of Hypertension, 2019, 37(2):229-252

Ehlers-Danlos Syndromes (EDs)

Former nomenclature and other names	Villefranche nomenclature	New Nomenclature	OMIM condition	Locus	Gene	OMIM gene	Protein	IP
GROUP A: Disorders of collagen primary structure and collagen processing								
Gravis/EDS I	Classical type	Classical EDS (cEDS)	130000	9q34.3	*COL5A1*	120215	Type V collagen	AD
Mitis/EDS II			130010	2q32.2	*COL5A2*	120190	Type V collagen	
				17q21.33	*COL1A1*	120150	Type I collagen (p. Arg312Cys)	
Arterial-Ecchymotic EDS	Vascular type	Vascular EDS (vEDS)	130050	2q32.2	*COL3A1*	120180	Type III collagen	AD
EDS IV				17q21.33	*COL1A1*	120150	Type I collagen p.(Arg312Cys) p.(Arg574Cys) p.Arg1093Cys)	
Arthrochalasis Multiplex Congenita	Arthrochalasia type	Arthrochalasia EDS (aEDS)	130060	17q21.33	*COL1A1*	120150	Type I collagen	AD
EDS VIIA			130060	7q21.3	*COL1A2*	120160		
EDS VIIB								
Human dermatosparaxis EDS VIIC	Dermatosparaxis type	Dermatosparaxis EDS (dEDS)	225410	5q35.3	*ADAMTS2*	604539	ADAMTS-2	AR
Cardiac-valvular EDS	/	Cardiac-valvular EDS (cvEDS)	225320	7q21.3	*COL1A2*	120160	Type I collagen Total absence of pro α2(I) collagen chains	AR

Am J Med Genet C Semin Med Genet. 2017 Mar;175(1):8-26

Ehlers-Danlos Syndromes (EDS)

Former nomenclature and other names	Villefranche nomenclature	New Nomenclature	OMIM condition	Locus	Gene	OMIM gene	Protein	IP
GROUP B: Disorders of collagen folding and collagen cross-linking								
Ocular-Scoliotic EDS	Kyphoscoliosis type	Kyphoscoliotic EDS (kEDS-*PLOD1*)	225400	1p36.22	*PLOD1*	153454	Lysylhydroxylase 1	AR
EDS VI								
EDS VIA								
/	/	Kyphoscoliotic EDS (kEDS-*FKBP14*)	614557	7p14.3	*FKBP14*	614505	FKBP22	AR
GROUP C: Disorders of structure and function of myomatrix, the interface between muscle and ECM								
		Classical-like EDS (clEDS)	606408	6p21.33-p21.32	*TNXB*	600985	Tenascin XB	AR
/	/	Myopathic EDS (mEDS)	616471	6q13-q14	*COL12A1*	120320	Collagen XII	AD/AR
GROUP D: Disorders of glycosaminoglycan biosynthesis								
EDS Progeroid	EDS Progeroid type	Spondylodysplastic EDS (spEDS-*B4GALT7*)	130070	5q35.3	*B4GALT7*	604327	Galactosyltransferase I β4GalT7	AR
	EDS Progeroid type 1							
EDS Progeroid type 2	β3GalT6-deficient EDS	Spondylodysplastic EDS (spEDS-*B3GALT6*)	615349	1p36.33	*B3GALT6*	615291	Galactosyltransferase II β3GalT6	AR
β3GalT6-deficient EDS								
Adducted Thumb Clubfoot syndrome		Musculocontractural EDS (mcEDS-*CHST14*)	601776	15q15.1	*CHST14*	608429	Dermatan-4 sulfotransferase-1	AR
EDS Kosho type		Musculocontractural EDS (mcEDS-*DSE*)	615539	6q22.1	*DSE*	605942	Dermatan sulfate epimerase-1	AR
EDS Musculocontractural type								
D4ST1-deficient EDS								

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Ehlers-Danlos Syndromes (EDS)

Former nomenclature and other names	Villefranche nomenclature	New Nomenclature	OMIM condition	Locus	Gene	OMIM gene	Protein	IP
GROUP E: Disorders of complement pathway								
EDSVIII	EDS periodontitis	Periodontal EDS (pEDS)	130080	12p13.31	*C1R*	613785	C1r	AD
					C1S	120580	C1s	
GROUP F: Disorders of intracellular processes[a]								
Spondylocheirodysplastic EDS		Spondylodysplastic EDS (spEDS-*SLC39A13*)	612350	11p11.2	*SLC39A13*	608735	ZIP13	AR
Brittle Cornea Syndrome		Brittle Cornea Syndrome (BCS)	229200	16q24	*ZNF469*	612078	ZNF469	AR
			614170	4q27	*PRDM5*	614161	PRDM5	AR
Unresolved forms of EDS								
Hypermobile EDS III	Hypermobility type	Hypermobile EDS (hEDS)	130020	?	?		?	AD
Conditions not included in EDS spectrum anymore								
Occipital horn syndrome	/	/	304150	Xq21.1	*ATP7A*	300011	ATP7A	X-L
Fibronectin-deficient (EDS X)	/	/						AD
Familial Articular hypermobility (EDS XI)	/	/						AD
X-linked EDS with muscle hematoma (EDS V)	/	/						X-L
Filamin A related EDS with periventricular nodular heterotopia	/	/	300049	Xq28	*FLNA*	300017	Filamin A	X-L

IP, inheritance pattern; AD, autosomal dominant; AR, autosomal recessive; X-L, X-linked recessive.

[a]For EDS subtypes implemented in this category, the underlying pathophysiological mechanism is not readily understood, and classification within this subgroup is provisionary, until further functional information becomes available.

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Ehlers-Danlos Syndromes (EDS)

A family history of the disorder, arterial rupture, or dissection in individuals less than 40 years of age, unexplained sigmoid colon rupture, or spontaneous pneumothorax in the presence of other features consistent with vEDS should all lead to diagnostic studies to determine if the individual has vEDS.

- Inheritance
  Autosomal dominant
- Major criteria
  1. Family history of vEDS with documented causative variant in *COL3A1*
  2. Arterial rupture at a young age
  3. Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology
  4. Uterine rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears
  5. Carotid–cavernous sinus fistula (CCSF) formation in the absence of trauma

- Minor criteria
  1. Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back
  2. Thin, translucent skin with increased venous visibility
  3. Characteristic facial appearance
  4. Spontaneous pneumothorax
  5. Acrogeria
  6. Talipes equinovarus
  7. Congenital hip dislocation
  8. Hypermobility of small joints
  9. Tendon and muscle rupture
  10. Keratoconus
  11. Gingival recession and gingival fragility
  12. Early onset varicose veins (under age 30 and nulliparous if female)

Am J Med Genet C Semin Med Genet. 2017 Mar;175(1):8-26

Ο ασθενής μας …

1. **Είναι άνδρας**
2. **Είναι 73 ετών**
3. **Η ΑΠ ήταν καλά ρυθμισμένη με < 3 αντιυπερτασικά φάρμακα**
4. **Χρειάζεται αγγειοσυσπαστικά**
5. **Δεν προϋπάρχει γνωστό ανεύρυσμα**
6. **Αρνητικό οικογενειακό ιστορικό**

N Engl J Med 2014; 371:e11August 21, 2014

Επομένως …

Αληθή ανευρύσματα

- Ινομυώδης δυσπλασία
- Σύνδρομο *Ehlers– Danlos*

N Engl J Med 2014; 371:e11August 21, 2014

Ενδοπαρεγχυματικά

- Οζώδης πολυαρτηρίτιδα
- Νευροϊνωμάτωση

Νευροϊνωμάτωση

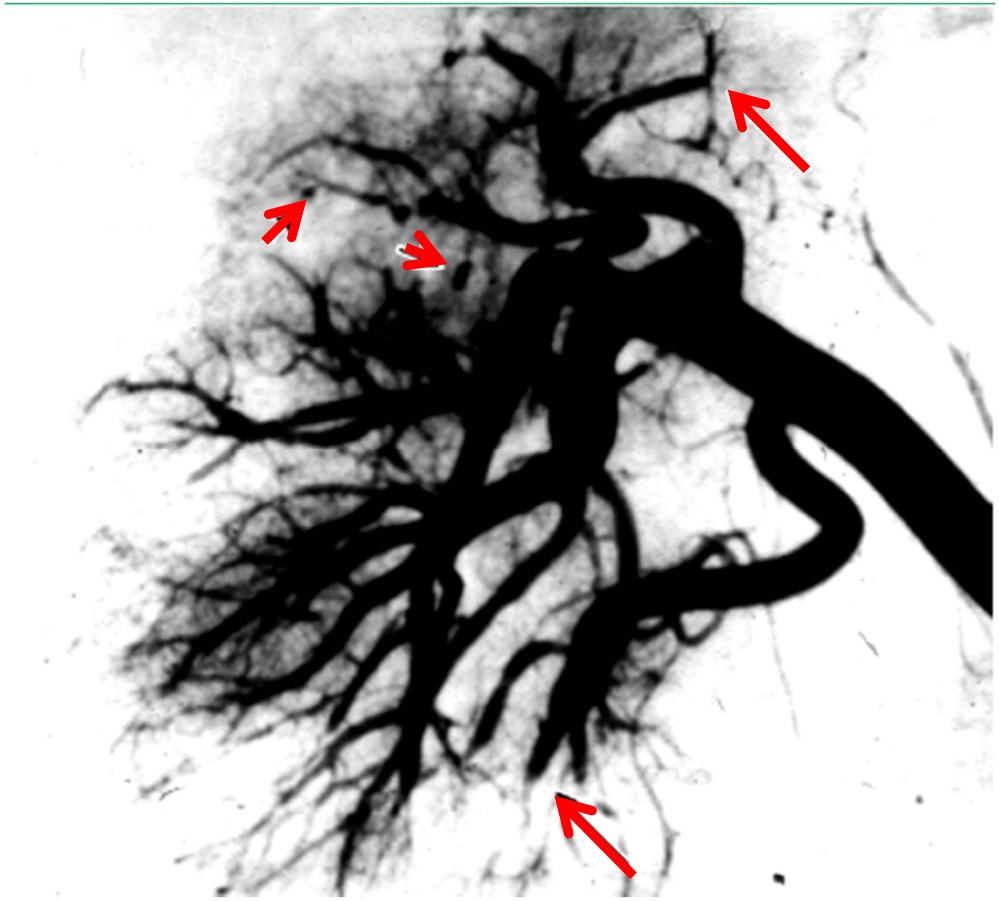
Disorder	Criteria
Schwannomatosis	Definite: Age > 30 years AND two or more nonintradermal schwannomas, at least 1 with histological confirmation AND no evidence of vestibular tumor on high-quality MRI scan AND no known constitutional NF2 mutation OR One pathologically confirmed nonvestibular schwannoma plus a first-degree relative who meets above criteria Possible: Age < 30 years AND two or more nonintradermal schwannomas, at least 1 with histological confirmation AND no evidence of vestibular tumor on high-quality MRI scan AND no known constitutional NF2 mutation OR Age > 45 years AND two or more nonintradermal schwannomas, at least 1 with histological confirmation AND no symptoms of 8th nerve dysfunction AND no known constitutional NF2 mutation OR Radiographic evidence of a nonvestibular schwannoma and first degree relative meeting criteria for definite Individuals with either unilateral vestibular schwannoma or multiple meningiomas together with one of the above tumors should be further evaluated for NF2

Korf BR, Handb Clin Neurol., 2013;111:333-40.

Οζώδης πολυαρτηρίτιδα (PAN)

Συστηματική νεκρωτική αγγειίτιδα των μικρών και μέσου μεγέθους μυϊκών αρτηριών

Criterion
1. Weight loss ≥4 kg
2. Livedo reticularis
3. Testicular pain or tenderness
4. Myalgias, weakness, or leg tenderness
5. Mononeuropathy or polyneuropathy
6. Diastolic BP >90 mm Hg
7. Elevated BUN or creatinine
8. Hepatitis B virus
9. Arteriographic abnormality
10. Biopsy of small or medium-sized artery containing PMN



Lightfoot RW Jr, Michel BA, Bloch DA, et al; Arthritis Rheum. 1990;33(8):1088

UpToDate®

Ο ασθενής μας …

1. **Δεν πληροί κανένα κριτήριο για PAN**
2. **Δεν πληροί κανένα κριτήριο για NF1**
3. **Όχι ενδοπαρεγχυματικό- αρνητικός απεικονιστικός έλεγχος**

N Engl J Med 2014; 371:e11August 21, 2014

Επομένως …

Ενδοπαρεγχυματικά

- Οζώδης πολυαρτηρίτιδα
- Νευροϊνωμάτωση

N Engl J Med 2014; 371:e11August 21, 2014

Στον ασθενή μας …

Ψευδή ανευρύσματα

- ~~Τραύμα~~
- ~~Ιατρογενή~~
- Αυτόματο
- Διαχωρισμός
- Μυκωτικό
- Νόσος Kawasaki

N Engl J Med 2014; 371:e11August 21, 2014

Νόσος Kawasaki

– Πυρετός διάρκειας τουλάχιστον 5 ημερών και τουλάχιστον 4 από τα παρακάτω 5 κλινικά γνωρίσματα
– Πολύμορφο δερματικό εξάνθημα (όχι πετέχειες ή φυσαλλιδώδεις βλάβες)
– Αμφοτερόπλευρη μη εξιδρωματική επιπεφυκίτις
– Ερύθημα στα χείλη και τη στοματική κοιλότητα
– Ερύθημα και οίδημα των άκρων με μεμβρανώδη απολέπιση των δακτύλων
– Τραχηλική λεμφαδενοπάθεια, συνήθως μονόπλευρη (με αδένα >1.5 εκ)

Franquelin, Jean Augustin (1798-1839); Medium: oil on canvas. Date: 19th Century. Hamburger Kunsthalle, Hamburg, Germany.

Burns JC, GlodéMP , Kawasaki Syndrome, Lancet. 2004;364(9433):533

Επομένως …

Ψευδή ανευρύσματα

- ~~Αμβλύ τραύμα~~
- ~~Ιατρογενή~~
- Αυτόματο
- Διαχωρισμός
- Μυκωτικό
- ~~Νόσος Kawasaki~~

N Engl J Med 2014; 371:e11August 21, 2014

Διαχωρισμός νεφρικής αρτηρίας

Almost ***200*** cases of spontaneous renal artery dissection have been published in the literature.

The etiology is certain, whether from the ***natural extension of aortic dissection***, as a ***consequence of percutaneous angioplasty***, or as a result of ***blunt abdominal trauma.***

Usually is observed in otherwise ***healthy men in the fourth to sixth decade of life*** and occurs in a 4:1 male to female ratio.

Kanofsky JA, Lepor H; Rev Urol. 2007 Summer;9(3):156-60

Διαχωρισμός νεφρικής αρτηρίας

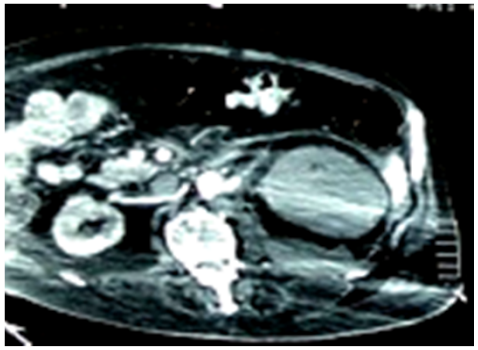
Conditions associated with the development of renal artery dissection***: fibromuscular dysplasia, malignant hypertension, severe atherosclerosis, Marfan syndrome, Ehlers-Danlos syndrome, subadventitial angioma, cystic medial necrosis, and extreme physical exertion***.

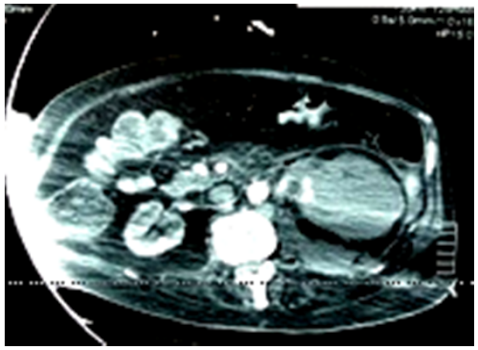
Clinical manifestations of renal artery dissection: ***progressive renovascular hypertension***, ***changes in renal function***, and ***symptoms of kidney infarction***.

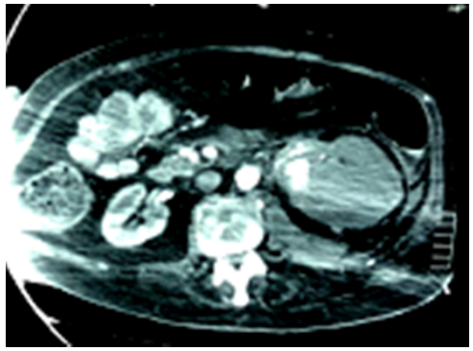
CT often shows areas of infarction, suggesting a vascular etiology. ***Angiography is the most useful test***, because it can precisely demonstrate the extent and nature of the vascular involvement while identifying potential treatment options.

Kanofsky JA, Lepor H; Rev Urol. 2007 Summer;9(3):156-60

Στον ασθενή μας ...







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Επομένως …

Ψευδή ανευρύσματα

- ~~Αμβλύ τραύμα~~
- ~~Ιατρογενή~~
- Αυτόματο
- ~~Διαχωρισμός~~
- Μυκωτικό
- ~~Νόσος Kawasaki~~

N Engl J Med 2014; 371:e11August 21, 2014

Μυκωτικό ανεύρυσμα

THE GULSTONIAN LECTURES,
on
MALIGNANT ENDOCARDITIS.

Delivered at the Royal College of Physicians of London, March, 1885.

By WILLIAM OSLER, M.D.,
Professor of Clinical Medicine at the University of Pennsylvania, Philadelphia.

Lecture I.

Mr. President and Gentlemen,—It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what

use to describe the grave form, and it expresses well an anatomical feature present in a large proportion of cases; but in others it is very inapplicable, as there may be no actual loss of substance, and no more destruction than occurs in the verrucose form; and, on the other hand, there may be great destruction and ulceration from causes of an entirely different nature. The numerous other terms employed—septic, infectious, diphtheritic, mycosis endocardii, arterial pyæmia—while each expressing some special feature, and so far suitable, have never come into very general use. On the whole, it seems to me that the names simple and malignant, which we use often to separate the milder and severe forms of many diseases, might appropriately be employed in describing the cases of acute endocarditis; the simple being those with few or slight symptoms, and which run a favourable course; the malignant, the cases with severe constitutional disturbance and extensive valve-lesions, whether ulcerative or vegetative, the term being more clinical than anatomical.

of the size of a billiard-ball. The small ones were not noticeable as aneurysms from the internal surface, but presented the appearance of fresh fungous vegetations, on separating which little slits could be seen leading to saccular dilatations of the middle and outer coats. The large aneurysm was thin-walled, with no laminated fibrine, and presented at the edges of the orifice and over the whole lining membrane of the sac many greyish-green vegetations, some of which had perforated the sac and caused a rupture into the pericardium. It may be presumed that, in this instance, the ulcerations led directly to the production of the aneurysms, certainly in the case of the smaller ones; and the larger sac presented a condition of mycotic endarteritis unique in my experience of aortic aneurysms.

Of associated pathological changes, we have, in the first place, those connected with some primary disease, to which the endocarditis

Μυκωτικό ανεύρυσμα

Προδιαθεσικοί παράγοντες:

- Εμβολισμός του αορτικού τοιχώματος με σηπτικά έμβολα που προέρχονται κυρίως από βακτηριακή ενδοκαρδίτιδα- Προηγηθείσα λοίμωξη (πνευμονία, χολοκυστίτιδα, λοίμωξη ουροποιητικού, οστεομυελίτιδα, λοίμωξη μαλακών μορίων, κλπ)

- Ενδοφλέβιες ενέσεις με επιμολυνθέν υλικό, το οποίο ενοφθαλμίζεται στο αορτικό τοίχωμα (ivdu) ή μετά από ιατρογενείς παρεμβάσεις (καθετηριασμός, τοποθέτηση ΚΦΓ, κλπ).

- Ανοσοανεπάρκεια (κίρρωση, γλυκοκορτικοειδή, κακοήθεια, χημειοθεραπεία, διαβήτης, κλπ)

- Αθηρωμάτωση

- Προϋπάρχον ανεύρυσμα

Μυκωτικό ανεύρυσμα

Δημιουργείται μετά από επιμόλυνση του αορτικού τοιχώματος:

- Απευθείας ενοφθαλμισμό (ιατρογενώς, ivdu)
- Βακτηριακή διασπορά (σε τραυματισμό του αρτηριακού τοιχώματος, αθηρωμάτωση, ανεύρυσμα)
- Κατά συνέχεια ιστού (απόστημα, μετεγχειρητική επιπλοκή)
- Σηπτικά έμβολα (ενδοκαρδίτιδα)

Μυκωτικό ανεύρυσμα

Αιτιολογικοί παράγοντες:

Staphylococcus aureus/methicillin-resistant *S. aureus* (MRSA)
Staphylococcus epidermidis
Salmonella spp.
Streptococcus pneumoniae
Treponema pallidum
Mycobacterium spp.
Coxiella burnetii

Pseudomonas, *Klebsiella*, *E.coli*, *Campylobacter*, *Yersinia, Brucella, Haemophilus influenzae, Acinetobacter*

Candida spp.
Cryptococcus spp.
Aspergillus spp.
Pseudallescheria boydii
Scedosporium apiospermum

Στον ασθενή μας …

1.Ατομικό αναμνηστικό (ΣΔτ2, αθηρωμάτωση)

2.Εγκαυματίας – πολλαπλά χειρουργεία (λοίμωξη μαλακών μορίων)

3.Επαναλαμβανόμενα σηπτικά shock (βακτηριαιμίες)

4.Στεφανιογραφία (ιατρογενής παρέμβαση)

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Συνοψίζοντας…

Εάν όχι αυτόματο, τότε πιθανώς μυκωτικό

N Engl J Med 2014; 371:e11August 21, 2014

Συνοψίζοντας…

Και εάν ληφθεί υπόψη:

- Pip-Tazo
- Daptomycin
- Meropenem
- Colistin
- Tigecycline
- Amikacin
- Anidulafungin
- Aztreonam
- Ceftazidime/avibactam

Αναμονή αιμοκαλλιεργειών, ιστική καλλιέργεια, παθολογοανατομική έκθεση

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ΕΥΧΑΡΙΣΤΩ

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